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(54) Method for producing an alcohol

Verfahren zur Herstellung eines Alkohols

Procédé pour la préparation d'un alcool

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AL: "New catalytic system for the hydrogenation
of ketones"

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Description

[0001] The present invention relates to a method for producing an alcohol. More particularly, the present invention relates to a novel method for efficient production at a high yield of alcohol useful as medical drugs, agricultural chemicals, various other chemicals or raw materials or a synthetic intermediate thereof, and to a new method for producing optically active alcohol, which is excellent in practicability and having various uses including synthetic intermediates of medical drugs and materials, for liquid crystal.

[0002] Methods for producing alcohol have been conventionally known, which comprise hydrogenation of carbonyl compounds, by using a homogeneous catalyst system, thereby obtaining the corresponding alcohol, including for example: (1) a method using a ruthenium complex as described in Comprehensive Organometallic Chemistry, Vol 4, p. 931 (1982), Eds. G. Wilkinson, F.G.A. Stone and E.W. Abel; (2) methods using a rhodium complex as described in Inorg. Nucl. Chem. Letters, Vol. 12, p. 865(1976); J. Organomet. Chem., Vol. 129, p. 239 (1997); Chem. Letters, P. 261 (1982); and Tetrahedron Letters, Vol 35, p. 4963 (1994); and (3) a method using an iridium complex as described in J. Am. Chem. Soc., Vol. 115, p. 3318 (1993).

[0003] However, these conventional methods require as a catalyst any of such metals as ruthenium, rhodium, iridium, palladium and platinum, which are relatively expensive noble metals, and the metals have problems in that the hydrogenation activity is low and the reaction requires specific conditions including a relatively high temperature or a high hydrogen pressure, thus making these materials unsuitable for practical use.

[0004] Additionally, the conventionally known methods for asymmetrically synthesizing optically active alcohol include: 1) a method using an enzyme such as baker's yeast, and 2) a method for asymmetric hydrogenation of a carbonyl compound by the use of a metal complex catalyst. Particularly, regarding the latter method, many cases of asymmetric catalytic reactions have been reported, including for example: (1) a method of asymmetric hydrogenation of a carbonyl compound having a functional group using optically active ruthenium catalyst described in detail in Asymmetric Catalysis In Organic Synthesis, p. 56-82 (1994) ed. R. Noyori; (2) a method based on hydrogen transfer type reduction reaction through asymmetric complex catalysis of ruthenium, rhodium and iridium described in Chem. Rev., Vol. 92, p. 1051-1069 (1992); (3) a method of asymmetric hydrogenation using a nickel catalyst prepared by modifying tartaric acid described in Petr. Chem., p. 882-831 (1980) and Advances in Catalysis, Vol. 32, p. 215 (1983) ed. Y. Izumi; (4) a method based on asymmetric hydrosilation as described in Asymmetric Synthesis, Vol. 5, Chap. 4 (1985) ed. J.D. Morrison and J. Organomet. Chem., Vol. 346, p. 413-424 (1988); and a method of borane-reduction in the presence of chiral ligands described in J. Chem. Soc., Perkin Trans. 1, p. 2039-2044 (1985) and J. Am. Chem. Soc., Vol. 109, p. 5551-5553 (1987).

[0005] Although the method using an enzyme gives alcohol with a relatively high optical purity, however, it is defective in that the kinds of reaction substrates are limited, and the resultant alcohol is limited to one having a specific absolute configuration. In the case of the method using an asymmetric hydrogenation catalyst based on a transition metal, while realising production of optically active alcohol with a high selectivity for such a substrate as keto acid, for example, it has a drawback of a low reaction rate, and in addition, the method is not valid for relatively simple carbonyl compounds having no functional group in the molecule.

[0006] For these reasons, there has been a demand for the achievement of a new synthetic method for producing an optically active alcohol having a high generality and using a highly active catalyst.

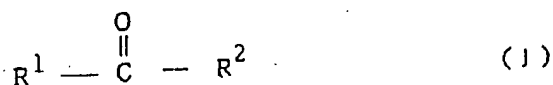
[0007] The present invention has therefore an object to solve these problems in the prior art, and provide a novel method for producing an alcohol through a hydrogenation reaction with a high efficiency by the use of an inexpensive catalyst system.

[0008] As means to solve the above-mentioned problems, the present invention provides a method for producing an alcohol, which comprises the step of causing a carbonyl compound to react with hydrogen in the presence of a homogeneous hydrogenation catalyst which is a transition metal complex catalyst of a group VIII metal, a base and a nitrogen-containing organic compound, wherein said nitrogen-containing organic compound is:

a) a mono-amine selected from primary amine, secondary amine or tertiary amine represented by the formula $\text{NR}^8\text{R}^9\text{R}^{10}$; or

b) a diamine represented by the formula $\text{R}^{11}\text{R}^{12}\text{N-Z-NR}^{13}\text{R}^{14}$ (wherein $\text{R}^8, \text{R}^9, \text{R}^{10}, \text{R}^{11}, \text{R}^{12}, \text{R}^{13}$ and R^{14} are each hydrogen, or are the same or different moieties selected from alkyl, cycloalkyl, aryl having 1 to 10 carbon atoms, and cyclic diamine; and Z is a group selected from alkylene, cycloalkylene and arylene having 1 to 6 carbon atoms).

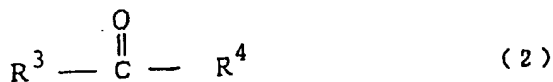
[0009] As the carbonyl compound which is the raw material for producing an alcohol through hydrogenation reaction, for example, a compound expressed by the following formula (1):



(where R¹ and R² are hydrogen, aromatic monocyclic or polycyclic hydrocarbon groups or hetero-monocyclic or polycyclic groups containing heteroatoms, which may have the same or different substitution groups or a saturated or unsaturated chain or cyclic hydrocarbon groups;

R¹ and R² together with the C-atom to which they are attached may also form a cyclic group) may appropriately be used.

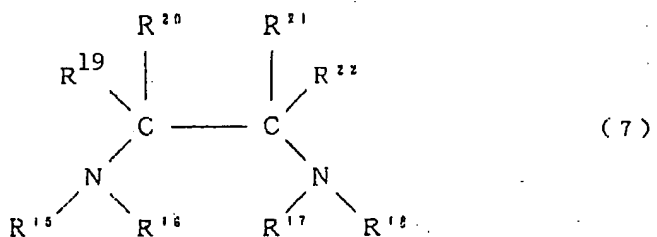
[0010] The present invention also provides a method for producing an optically active alcohol, which comprises the step of subjecting a carbonyl compound expressed by the following general formula (2):



(where, R³ is an aromatic monocyclic or polycyclic hydrocarbon group, a saturated or unsaturated aliphatic or cyclohydrocarbon group, or a hetero-monocyclic or polycyclic group containing heteroatoms, which may have a substitution group; and R⁴ is a saturated or non-saturated chain, cyclic or aromatic cyclic hydrocarbon or heterocyclic group, which may have hydrogen or a substitution group. R³ and R⁴ together with the C-atom to which they are attached may also form cyclic groups) to a hydrogenation reaction in the presence of an asymmetric hydrogenation catalyst which is a transition metal complex catalyst of a group VIII metal, and an optically active nitrogen-containing compound, wherein said nitrogen-containing compound is

a) an optically active monoamine in which at least one of the substitution groups is an optically active group and those remaining include hydrogen, or saturated or unsaturated hydrocarbon group or aryl group, or

b) an optically active diamine compound represented by the following general formula (7):



(wherein, R¹⁵, R¹⁶, R¹⁷ and R¹⁸ are hydrogen or saturated or unsaturated hydrocarbon group, aryl group, urethane group or sulfonyl group, and R¹⁹, R²⁰, R²¹ and R²² are the same or different groups such that carbon atoms bonded with these substitution groups form centers of asymmetry, and represent hydrogen or alkyl group, aromatic monocyclic or polycyclic, saturated or unsaturated hydrocarbon group, and cyclic hydrocarbon group), and a base, thereby producing an optically active alcohol expressed by the following general formula (3):



(where R³ and R⁴ are the same organic groups as above).

[0011] Regarding the present invention for a method of producing an alcohol, as the substitution group in the case of formula (1), any of various organic groups which never impair the hydrogenation reaction, such as hydrocarbon group, halogen group, hydroxy group, alkoxy group, carboxyl group, ester group, amino group and heterocyclic group may appropriately be used.

[0012] As R¹ and R², applicable moieties include hydrogen atom; aromatic monocyclic or polycyclic groups such as phenyl group, 2-methylphenyl, 2-ethylphenyl, 2-isopropylphenyl, 2-tert-butylphenyl, 2-methoxyphenyl, 2-chlorophenyl, 2-vinylphenyl, 3-methylphenyl, 3-ethylphenyl, 3-isopropylphenyl, 3-methoxyphenyl, 3-chlorophenyl, 3-vinylphenyl, 4-methylphenyl, 4-ethylphenyl, cumenyl, mesityl, xylyl, 1-naphthyl, 2-naphthyl, anthryl, phenanthryl, and indenyl; heteromonocyclic or polycyclic groups such as thienyl, furyl, pyranyl, xanthenyl, pyridyl, imidazolyl, indolyl, and phenanthrolyl; and ferrocenyl group, cyclic or acyclic hydrocarbon groups, for example, alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, hexyl, and heptyl, cycloalkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, and unsaturated hydrocarbons such as benzyl, vinyl and allyl. R¹ and R² together with the C-atom to which they are attached may also form acyclic group. Examples of such cyclic groups are saturated or unsaturated cyclo-aliphatic groups providing cyclic ketone such as cyclopentanone, cyclohexanone, cycloheptanone, cyclopentenone, cyclohexenone, cycloheptenone; substituted saturated or unsaturated cyclo-aliphatic groups having substitution groups selected from alkyl, aryl, unsaturated alkyl, aliphatic or cyclo-aliphatic group containing hetero atom.

[0013] The group VIII, metals include rhodium (Rh), ruthenium (Ru), iridium (Ir), palladium (Pd), and platinum (Pt). Particularly, ruthenium (Ru) is used for a high activity in the present invention for producing an alcohol.

[0014] These group VIII metals are used in the form of soluble complex catalyst as homogeneous catalyst. For example, this catalyst can be expressed by the following general formula (4).



(where, M is a group VIII metal; X is halogen atom, carboxyl group, alkoxy group or hydroxy group; and L is phosphine, olefin, diolefin, cycloolefin, CO, arsine, amine or other organic ligand)

[0015] For example, phosphine ligand can be expressed by a general formula PR⁵R⁶R⁷, where R⁵, R⁶, and R⁷ may be the same or different, and are aliphatic groups, alicyclic groups or aromatic groups, or may be bidentate phosphine ligands. Applicable phosphine ligands include, for example, such tert-phosphines as trimethylphosphine, triethylphosphine, tributylphosphine, triphenylphosphine, tricyclohexylphosphine, tri(p-tolyl)phosphine, diphenylmethylphosphine, dimethylphenylphosphine, and bidentate tert-phosphine compounds such as bis-diphenylphosphinoethane, bis-diphenylphosphinopropane, bisdiphenylphosphinobutane, bis-dimethylphosphinoethane, and bis-dimethylphosphinopropane.

[0016] As a complex based on the ligands described above, preferable examples include complexes of ruthenium, rhodium, iridium, palladium and platinum. Among others, ruthenium complex has a high activity. More specifically, applicable complexes include RuCl₂[P(C₆H₅)₃]₄, RuCl₂[P(C₆H₅)₃]₃, RuH₂[P(C₆H₅)₃]₄, RuHCl[P(C₆H₅)₃]₄, RuH(HCOO)[P(C₆H₅)₃]₃, RuH(CH₃COO)[P(C₆H₅)₃]₃, RuCl₂[P(CH₃)(C₆H₅)₂]₄, RuCl₂[(C₆H₅)₂P(CH₂)₂P(C₆H₅)₂]₂, RuCl₂[P(CH₃)₃]₄, RuHCl[P(CH₃)₃]₄, RuBr₂[P(C₆H₅)₃]₄, and RuI₂[P(C₆H₅)₃]₄. It is needless to mention that the complexes applicable are not limited to those enumerated above.

[0017] The amount of the group VIII transition metal complex for the method of production of an alcohol, varying with the reactor volume and economic merits, can be at a ratio within a range of from 1/100 to 1/100,000 in mole ratio, or more preferably, within a range of from 1/500 to 1/100,000 in mole ratio relative to the carbonyl compound which is the reaction raw material.

[0018] Bases applicable in the present invention include inorganic and organic bases. In the bases expressed by the general formula MY, for example, M is an alkali metal or an alkaline earth metal, and Y is a hydroxy group, alkoxy group, mercapto group or naphthyl group, and more specifically, applicable compounds include KOH, KOCH₃, KOCH(CH₃)₂, KC₁₀H₈, KOC(CH₃)₃, LiOH, LiOCH₃, and LiOCH(CH₃)₂, NaOH, NaOCH₃, NaOCH(CH₃)₂ as well as quaternary ammonium salt.

[0019] The amount of the base as described above should be within a range of from 0.5 to 10,000 equivalents, or more preferably, from 2 to 40 equivalents relative to the group VIII transition metal complex.

[0020] As the nitrogen-containing organic compound used in the present invention, the following amine compounds are typical example: mono amine compounds such as methylamine, ethylamine, propylamine, butylamine, pentylamine, hexylamine, cyclopentylamine, cyclohexylamine, benzylamine, dimethylamine, diethylamine, dipropylamine, dihexylamine, dicyclopentylamine, dicyclohexylamine, dibenzylamine, diphenylamine, phenylethylamine, piperidine and piperadine; and diamine compounds such as methylenediamine, ethylenediamine, 1,2-diaminopropane, 1,3-diaminopropane, 1,4-diaminobutane, 2,3-diaminobutane, 1,2-cyclopentanediamine, 1,2-cyclohexanediamine, N-

methylethylenediamine, N,N'-dimethylethylenediamine, N,N,N'-trimethylethylenediamine, N,N,N',N'-tetramethylethylenediamine, o-phenylenediamine, and p-phenylenediamine.

[0021] The amount of these compounds should be within a range of from 1 to 1000 equivalents relative to the transition metal complex in the case of monoamine compound, or more preferably, from 2 to 4 equivalents, and within a range of from 0.5 to 2.5 equivalents in the case of diamine compound, or more preferably, from 1 to 2 equivalents.

[0022] The transition metal complex used as the catalyst, the base and the nitrogen-containing compound are indispensable for ensuring smooth progress of reaction. The absence of even any of these constituents makes it impossible to obtain a sufficient reaction activity.

[0023] In the present invention, furthermore, any liquid solvent which can dissolve the reaction raw materials and catalyst constituents may be used. Applicable solvents include aromatic hydrocarbon solvents such as toluene and xylene, aliphatic hydrocarbon solvents such as pentane and hexane, halogen-containing hydrocarbon solvents such as methylene chloride, ether type solvents such as ether and tetrahydrofuran, alcohol type solvents such as methanol, ethanol, 2-propanol, butanol, benzyl alcohol, and organic solvents containing heteroatoms such as acetonitrile, DMF and DMSO. Since the product is alcohol, alcohol type solvents are preferable. More preferably, 2-propanol may be preferably used. When the reaction substrate is hardly soluble in a solvent, a mixed solvent comprising those selected from those enumerated above may be used.

[0024] The amount of the solvent is determined from solubility of the reaction substrate and relative economic merits. In the case of 2-propanol, the reaction may be caused at a substrate concentration within a range of from a low concentration of under 1% to a state near the non-existence of solvent, but it is preferable to use it at a concentration within a range of from 20 to 50 wt%.

[0025] In the present invention, the hydrogenation sufficiently proceeds under 1 atm of hydrogen, because the catalyst has a very high activity. Taking account of economic merits, however, it should preferably be within a range of from $10 \cdot 10^4$ Pa - $10 \cdot 10^6$ Pa (1 to 100 atm), or more preferably, from $30 \cdot 10^4$ Pa - $50 \cdot 10^5$ Pa (3 to 50 atm). Considering economic merits for the process, it is possible to maintain a high activity even under a pressure of up to $10 \cdot 10^5$ Pa (10 atm).

[0026] The reaction temperature should preferably be within a range of from 15 to 100°C, while it is possible to cause the reaction at a temperature near the room temperature as within a range of from 25 to 40°C. However, the present invention is characterized in that the reaction proceeds even at a low temperature of from -100 to 0°C. The reaction is completed in a period of time within a range of from a few minutes to ten hours, depending upon such reaction conditions as reaction substrate concentration, temperature and pressure.

[0027] The reaction system in the present invention may be batch or continuous.

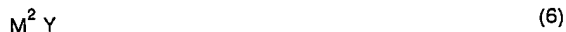
[0028] Now, the method of the present invention is described in further detail below by means of examples.

[0029] In addition, the present invention relating to the method for producing an optically active alcohol provides also an embodiment wherein the above-mentioned asymmetric hydrogenation catalyst is a complex of a group VIII metal; for example, a metal complex having an optically active ligand, one wherein the base is a hydroxide or a salt of an alkali metal or an alkaline earth metal, or a quaternary ammonium salt, and one wherein the optically active compound as a nitrogen-containing asymmetric compound is an optically active amine compound as described on p. 15.

[0030] An asymmetric hydrogenation catalyst can be expressed, for example, by the following general formula (5):



(where, M^I is a group VIII transition metal such as ruthenium, rhodium, iridium, palladium, or platinum; X is hydrogen, a halogen atom, a carboxyl group, a hydroxy group, or an alkoxy group, L is an optically active phosphine ligand or an optically active organic arsenic ligand; and m and n are integers), and the base may be a metal salt or a quaternary ammonium salt expressed by the following general formula (6):



(where, M^2 is an alkali metal or an alkali earth metal; and Y is hydroxy group, alkoxy group, mercapto group or naphthyl group).

[0031] The carbonyl compound which is the raw material in the present invention is expressed by the general formula (2). In this case, R^3 is a non-substituted or substituted aromatic monocyclic or polycyclic hydrocarbon group, a saturated or unsaturated aliphatic or cyclic-hydrocarbon group, or a hetero-monocyclic or polycyclic group containing heteroatoms such as nitrogen, oxygen or sulfur atoms, and applicable ones include, for example, aromatic monocyclic or polycyclic groups such as phenyl group, 2-methylphenyl, 2-ethylphenyl, 2-isopropylphenyl, 2-tert-butylphenyl, 2-meth-

oxyphenyl, 2-chlorophenyl, 2-vinylphenyl, 3-methylphenyl, 3-ethylphenyl, 3-isopropylphenyl, 3-methoxyphenyl, 3-chlorophenyl, 3-vinylphenyl, 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl, 4-tert-butylphenyl, 4-vinylphenyl, cumenyl, mesityl, xyllyl, 1-naphthyl, 2-naphthyl, anthryl, phenanthryl, and indenyl; and hetero-monocyclic or polycyclic groups such as thienyl, furyl, pyranyl, xanthenyl, pyridyl, imidazolyl, indolyl, carbazolyl, and phenanthrolyl. and ferrocenyl group such as thienyl, furyl, pyranyl, xanthenyl, pyridyl, imidazolyl, indolyl, carbazolyl, and phenanthrolyl.

5 R⁴ is a saturated or unsaturated hydrocarbon group, aryl group, or a functional group containing heteroatoms, and applicable ones include, for example, alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, hexyl and heptyl; cycloalkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl; and unsaturated hydrocarbon and other groups such as benzyl, vinyl and allyl. Furthermore, β -keto acid derivatives having a functional group at β -position are also applicable. R³ and R⁴ together with the C-atom to which they are attached may also form a cyclic group. Examples

10 of such cyclic groups are saturated or unsaturated cyclo-aliphatic groups providing cyclic ketone such as cyclopentanone, cyclohexanone, cycloheptanone, cyclopentenone, cyclohexenone, cycloheptenone; substituted saturated or unsaturated cyclo-aliphatic groups having substitution groups selected from alkyl, aryl, unsaturated alkyl, aliphatic or cyclo-aliphatic group containing hetero atom.

cyclo-aliphatic group containing hetero atom.
 [0032] In the transition metal complex expressed by the general formula (5) in the present invention, M¹ is a group
 VIII transition metal such as ruthenium, rhodium, iridium, palladium and platinum, and among others, ruthenium is
 particularly preferable. X is hydrogen, halogen atom, carboxyl group, hydroxyl group or alkoxy group. L is an optically
 active phosphine ligand and applicable ones include BINAP: 2,2'-bis-(diphenylphosphino)-1,1'-binaphthyl, BINAP de-
 rivative having alkyl group or aryl group connected to naphthyl ring, such as H₂BINAP; BINAP derivative having 1-5 alkyl
 substitution group(s) at site of aromatic ring on phosphorus atom, for example TolBINAP: 2,2'-bis-(di-p-tolylphosphino)-
 1,1'-binaphthyl, BICHEP: 2,2'-bis-(dicyclohexylphosphino)-6,6'-dimethyl-1,1'-biphenyl, BPPFA: 1-[1,2-bis(diphenyl-
 phosphino)ferrocenyl] ethyldimethylamine, CHIRAPHOS: 2,3-bis(diphenylphosphino) butane, CYCPHOS: 1-cy-
 clohexyl-1,2-bis(diphenylphosphino)ethane, DEGPPOS: substitution-3,4-bis(diphenylphosphino)pyrrolidine, DIOP:
 2,3-O-isopropylidene -2,3-dihydroxy-1,4-bis(diphenylphosphino)butane, DIPAMP: 1,2-bis[(O-methoxyphenyl phenyl-
 phosphino)ethane, DuPHOS: substituted-1,2-bis(phospholano) benzene, NORPHOS: 5,6-bis(diphenylphosphino)-
 2-norbornene, PNNP: N,N'-bis(diphenylphosphino)-N,N'-bis(1-phenylethyl) ethylenediamine, PROPHOS: 1,2-bis-
 (diphenylphosphino)propane, and SKEWPHOS: 2,4-bis(diphenylphosphino)pentane.

[0033] A bidentate phosphine ligand has an n of 1 or 2, and a monodentate phosphine ligand has an n of 1. It is needless to mention that the optically active phosphine ligand applicable in the present invention is not limited at all to these values, and the metal is not limited at all to ruthenium.

all to these values, and the metal is not limited at all to ruthenium.

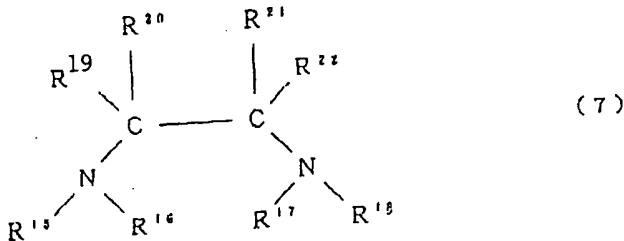
30 [0034] The amount of the group VIII, transition metal complex in the present invention, varying with the reactor, the reaction system and economic merits, can be at a ratio within a range of from 1/100 to 1/100,000 in mole ratio, or more preferably, within a range of from 1/500 to 1/10,000 in mole ratio relative to the carbonyl compound which is the reaction substrate.

[0035] In the base expressed by the general formula M^2Y used in the present invention, M^2 is an alkali metal or an alkali earth metal, and Y is hydroxy group, alkoxy group, mercapto group or naphthyl group, and more specifically, applicable ones include KOH , $KOCH_3$, $KOC(CH_3)_2$, $KOC(CH_3)_3$, $KC_{10}H_8$, $LiOH$, $LiOH_3$, and $LiOCH(CH_3)_2$, $NaOH$, $NaOC(CH_3)_3$, $NaOC(CH_3)_2$, as well as quaternary ammonium salt.

[0036] The amount of the base as described above should be within a range of from 0.5 to 100 equivalents, or more preferably, from 2 to 40 equivalents relative to the group VIII transition metal complex.

preferably, from 2 to 40 equivalents relative to the group VIII transition metal complex.

40 [0037] The nitrogen-containing compound used in the present invention is an optically active monoamine in which at least one of the substitution groups is an optically active group and the remaining ones include hydrogen, or saturated or unsaturated hydrocarbon group or aryl group, or an optically active diamine compound expressed by the following general formula (7):



(where, R¹⁵, R¹⁶, R¹⁷ and R¹⁸ are hydrogen or saturated or unsaturated hydrocarbon group, aryl group, urethane group

or sulfonyl group, and R¹⁹, R²⁰, R²¹ and R²² are the same or different groups such that carbons bonded with these substitution groups form centers of asymmetry, and represent hydrogen or alkyl group, aromatic monocyclic or polycyclic, saturated or unsaturated hydrocarbon group, and cyclic hydrocarbon group). Examples include such optically active diamine compounds as optically active 1,2-diphenylethylene diamine, 1,2-cyclohexanediamine, 1,2-cycloheptanediamine, 2,3-dimethylbutanediamine, 1-methyl-2,2-diphenylethylenediamine, 1-isobutyl-2,2-diphenylethylenediamine, 1-isopropyl-2,2-diphenylethylenediamine, 1-methyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-isobutyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-isopropyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-benzyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-methyl-2,2-dinaphthylethylenediamine, 1-isobutyl-2,2-dinaphthylethylenediamine, and 1-isopropyl-2,2-dinaphthylethylenediamine, and optically active diamine compounds in which one or both of the substitution groups R¹⁵ and R¹⁷ are sulfonyl group or urethane group. Optically active diamine compounds are not limited to the optically active ethylene-diamine derivatives enumerated above, but include also optically active propanediamine, butanediamine and phenylenediamine derivatives. The amount of these optically active amine compounds should be within a range of from 1 to 10 equivalents relative to the transition metal complex in the case of a monoamine compound, or more preferably, from 2 to 4 equivalents, and within a range of from 0.5 to 2.5 equivalents in the case of a diamine compound, or more preferably, from 1 to 2 equivalents.

[0038] In the present invention, it is important, in order to obtain a high optical yield, to achieve an appropriate combination of an absolute configuration of the optically active ligand and the absolute configuration of the optically active nitrogen-containing compound in the asymmetric hydrogenation catalyst as the catalyst component. The combination of S-phosphine ligand and S,S-diamine is, for example, best choice and gives (R)- alcohol. The combination of S-phosphine ligand and R,R-diamine, while the reaction proceeds, results in an extremely low optical yield.

[0039] The optical active transition metal complex, the base and the optical active nitrogen-containing compound used as catalyst component in the present invention as described above are indispensable for achieving a high optical yield. Lack of even any of these constituents makes it impossible to obtain alcohol with a sufficient optical activity and a high purity.

[0040] In the present invention, furthermore, any liquid solvent which can dissolve the reaction raw materials and catalyst components may be used. Applicable solvents include aromatic hydrocarbon solvents such as toluene and xylene, aliphatic hydrocarbon solvents such as pentane and hexane, halogen-containing hydrocarbon solvents such as methylene chloride, ether type solvents such as diethylether and tetrahydrofuran, alcohol type solvents such as methanol, ethanol, 2-propanol, butanol, benzyl alcohol, and organic solvents containing heteroatoms such as acetonitrile, DMF and DMSO. Since the product is alcohol, alcohol type solvents are preferable. More preferably, 2-propanol may be preferably used. When the reaction substrate is hardly soluble in a solvent, a mixed solvent comprising ones selected from those enumerated above may be used.

[0041] The amount of solvent is determined from solubility of the reaction substrate and relative economic merits. In the case of 2-propanol, the reaction may be caused at a substrate concentration within a range of from a low concentration of under 1% to a state near the non-existence of solvent, but it is preferable to use it at a concentration within a range of from 20 to 50 wt. %.

[0042] In the present invention, the hydrogenation sufficiently proceeds under 1 atm of hydrogen because the catalyst has a very high activity. Taking account of economic merits, however, it should preferably be within a range of from $10 \cdot 10^4$ - $10 \cdot 10^6$ Pa (1 to 100 atm), or more preferably, from $30 \cdot 10^4$ - $50 \cdot 10^5$ Pa (3 to 50 atm). Considering economic merits for the process as a whole, it is possible to maintain a high activity even under a pressure of up to 10 atm.

[0043] The reaction temperature should preferably be within a range of from 15 to 100°C, while it is possible to cause the reaction at a temperature near the room temperature as within a range of from 25 to 40°C. However, the present invention is characterized in that the reaction proceeds even at a low temperature of from -100 to 0°C. The reaction is completed in a period of time within a range of from a few minutes to ten hours, depending upon such reaction conditions as reaction substrate concentration, temperature and pressure. Now, the present invention is described in detail by means of examples.

[0044] The form of reaction in the present invention may be batch or continuous.

EXAMPLES

EXAMPLE 1

[0045] $\text{RuCl}_2[\text{P}(\text{C}_6\text{H}_5)_3]_3$ (9.6 mg, 0.01 mmol), KOH (0.02 mmol), ethylenediamine (0.01 mmol) and acetophenone (60 mg, 5.0 mmol) were dissolved into 3 ml of 2-propanol, and after deaeration for argon substitution, the resultant mixture was totally transferred into a glass autoclave of 100 ml. Then, hydrogen was charged into it until a prescribed pressure [$30 \cdot 10^4$ Pa (3 atm)] was achieved and reaction was started. After stirring the reaction mixture for 30 minutes, the reaction pressure was brought back to the atmospheric pressure. Phenethylalcohol was identified as the reaction product by gas chromatography and NMR analysis of the reaction mixture.

and the product was quantitatively measured. The reaction substrate was totally consumed, giving a phenetyl alcohol yield as the product of over 99%.

Examples 2 to 23

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[0046] Under the conditions shown in Example 1, with a reaction substrate changed from acetophenone, hydrogenation was conducted, and a corresponding alcohol compound was obtained substantially in a theoretical amount in each of these Examples. The raw material carbonyl compounds and the yields of the resultant compounds are shown in Tables 1 to 3.

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Table 1

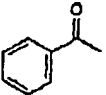
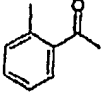
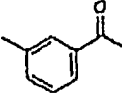
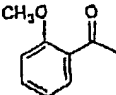
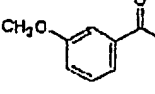
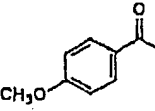

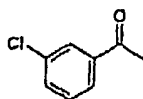
Example No.	(Reaction substrate) Raw material carbonyl compound	Product alcohol yield (%)
1		99
2		95
3		99
4		50
5		99
6		99
7		70

Table 2

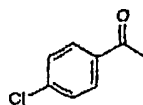
Example No.	(Reaction substrate) Raw material carbonyl compound	Product alcohol yield (%)
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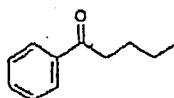
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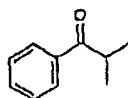
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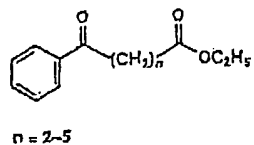
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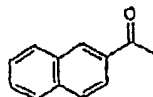
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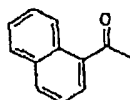
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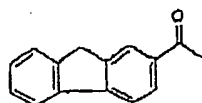
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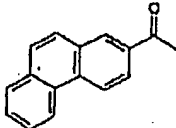
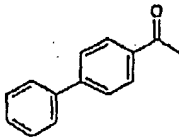
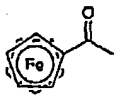
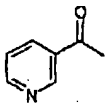
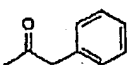
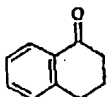
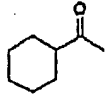
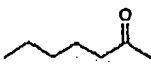
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Table 3

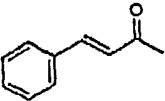

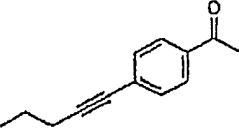
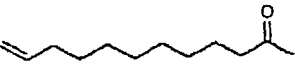
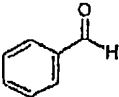
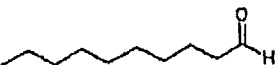
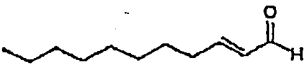
Example No.	(Reaction substrate) Raw material carbonyl compound	Product alcohol yield (%)
1 6		9 8
1 7		9 9
1 8		9 7
1 9		9 7
2 0		9 9
2 1		9 9
2 2		9 8
2 3		9 9

Example 24-30

[0047] Under the conditions shown in Example 1, hydrogenation reaction was conducted using unsaturated carbonyl compounds having a carbon-carbon double bond or a carbon-carbon triple bond. Corresponding alcohol compounds were obtained at high yields.

[0048] Carbon-carbon multiple bonds were not hydrogenated, and carbonyl groups only were hydrogenated. The results of above reaction are shown in Table 4.

Table 4

Example No.	Reaction substrate Raw material carbonyl compound	Products alcohol yield (%)
24		95
25		98
26		98
27		95
28		95
29		95
30		88

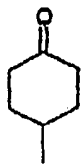
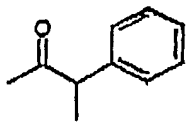
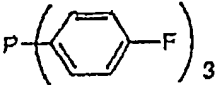
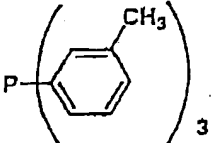
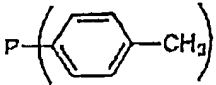
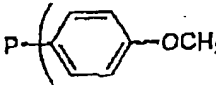
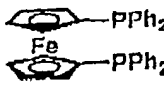
Example 31-39

[0049] Under the conditions shown in Example 1, with 4-methylcyclohexynone and 2-phenylmethylketone having chiral carbon atom groups in the molecular structure, the effects of added phosphine ligands were surveyed.

[0050] Each reaction provides quantitatively alcohol products. The resultant cis/trans ratio of alcohols derived from

4-methylcyclohexanone and syn/anti ratio of alcohol derived from 2-phenylmethylketone were shown in Table 5.

Table 5

Example No.	Phosphine ligand	<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  </div> <div style="text-align: center;">  </div> </div>	
		cls:trans	syn:anti
31	PPh ₃	92:8	14:86
32		93:7	22:78
33		92:8	6:94
34		92:8	5:95
35		93:7	4:96
36	dppe	70:30	24:76
37	dppp	74:26	15:85
38	dppb	88:12	8:92
39		82:18	24:76

Example 40

[0051] To prove the high activity of the catalyst of the present invention, the ratio of the reaction substrate to the catalyst was set to 5,000 and reaction was caused to determine the initial reaction rate.

[0052] More specifically, acetophenone (20 mol), RuCl₂ [P(C₆H₅)₃]₃ (3.8 mg, 0.004 mol), KOH (0.08 mol) and ethylenediamine (0.004 mol) were dissolved into 12 ml 2-propanol, and after deaeration and substitution with argon gas, the resultant mixture was totally transferred to a 500 ml glass autoclave. Hydrogen was then injected to a prescribed pressure [30·10⁴ Pa (3atm)] and reaction was started. The reaction was caused by direct connection to a hydrogen

cylinder so as to keep a constant hydrogen pressure. The reaction was completed in 80 minutes, and the initial rate of the reaction was determined to be 6,700 mol/Ru catalyst mol. hr.

Example 41

[0053] Reaction was conducted under the same conditions as in Example 1 except for a hydrogen pressure of $[10 \cdot 10^4$ Pa (1 atm)]. The initial rate was 880 mol/Ru catalyst mol.hr.

Example 42

[0054] Reaction was conducted under the same conditions as in Example 1 except for a hydrogen pressure of $[50 \cdot 10^5$ Pa (50 atm)]. The initial rate was 23, 000 mol/Ru catalyst mol. hr.

Example 43

[0055] Reaction was conducted under the same conditions as in Example 1 except for a reaction temperature of -20°C . The reaction was completed in ten hours and phenethylalcohol was obtained at a yield of 98%.

Comparative Example 1

[0056] Reaction was conducted under the same conditions as in Example 1 except that KOH and ethylene diamine were not added. The reaction rate was 5 mol/Ru catalyst mol. hr., and the reaction showed almost no progress.

Comparative Example 2

[0057] Reaction was conducted under the same conditions as in Example 1, but without adding ethylenediamine. The reaction rate was 70 mol./Ru catalyst mol. hr. even in the absence of hydrogen.

Comparative Example 3

[0058] Reaction was conducted under the same conditions as in Example 1, but without adding KOH. The reaction rate was 5 mol/Ru catalyst mol.hr., and the reaction showed almost no progress.

Comparative Example 4

[0059] Reaction was conducted under the same conditions as in Example 1., but without injecting hydrogen. The reaction rate was 8 mol/Ru catalyst mol.hr., and the reaction showed almost no progress.

Example 44

[0060] Reaction was conducted under the same conditions as in Example 1 except for the use of p-diacetylbenzene as a carbonyl compound. This gave p-bis(1-hydroxy)benzene was obtained at a yield of 99%.

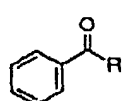
[0061] According to the present invention, as described above in detail, it is possible to manufacture alcohol from a carbonyl compound efficiently at a high yield.

[0062] The following examples show the present invention for producing optically active alcohols.

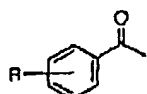
[0063] The applicable reaction substrates, optically active phosphines and diamine ligands as typical examples are shown in Table 6. and Table 7.

Table 6

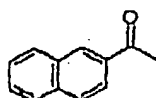
Carbonyl compound



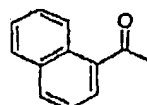
7a: R = CH₃
 7b: R = n-C₄H₉
 7c: R = (CH₂)₂CH



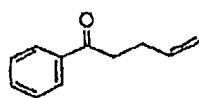
8a: R = CH₃
 8b: R = Cl
 8c: R = CH₃O
 8d: R = (CH₃)₂O



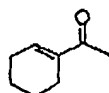
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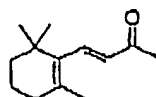
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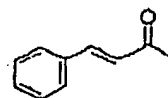
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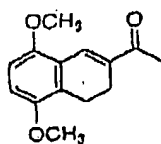
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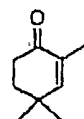
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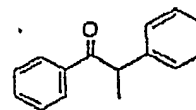
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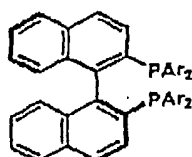
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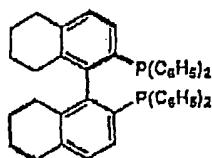
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Table 7

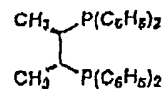
Phosphine ligands



(S)-1: Ar = C₆H₅
(BINAP)
(S)-2: Ar = p-CH₃C₆H₄
(TolBINAP)

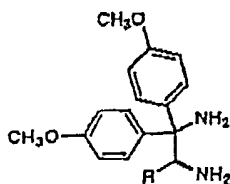
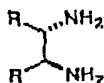


(R)-3
(H₈BINAP)



(2R,3R)-4
(CHIRAPHOS)

Diamine ligand



(S,S)-5: R = C₆H₅
(S,S)-6: R = C₆H₁₁
(S)-7: R = CH₃
(S)-8: R = (CH₃)₂CHCH₂
(S)-9: R = (CH₃)₂CH

Example 45

[0064] Into a Schlenk reaction tube, 0.5 M 2-propanol solution (40 μ L) of KOH, (S,S)-diphenylethylenediamine (2.1 mg, 0.01 mol), 1'-acetonaphthone (Compound 10 in Table 6) (85 mg, 5.0 mol) and 3 ml 2-propanol were charged in an argon gas flow. After deaeration and argon substitution, the reaction solution was adjusted by adding RuCl₂((S)-binap)(dmf)_n (9.6 mg, 0.01 mol). This solution was repeatedly subjected to deaeration and argon substitution to achieve complete dissolution, and then, the reaction was started by transferring the solution into a 100 ml glass autoclave and injecting hydrogen into it to a prescribed pressure. After stirring for six hours at 28°C, temperature was brought to the room temperature, and the reaction product was subjected to gas chromatography and, H NMR analysis to identify the product and determine reaction yield (higher than. 99%). Further, the optical purity of the resultant (R)-1-(1-naphthyl)-ethanol was determined by means of an optically active column from HPLC, the result being 97%ee.

Examples 46 to 58

[0065] In the same manner as in Example 45, the reaction was caused under the reaction conditions including optically active diamine, hydrogen pressure, temperature and reaction type with the carbonyl compounds as shown in Table 6 as the reaction substrates, and respective optically active alcohol products were obtained with high yields. The

results are shown in Table 8.

Table 8

Example	Carbonyl compound	Photoactive ligand		Reaction condition			Product	
		Phosphine	Diamine	H ₂ Pa (atm)	Temp. °C	Time, h	% yield	Ke _e config
46	7 a	(S)-1	(S)-8	40·10 ⁴ (4)	28	3	>99	87 R
47	7 b	(S)-1	(S)-7	" (4)	28	3	>99	90 R
48	7 c	(S)-2	(S)-9	80·10 ⁴ (8)	28	6	>99	95 R
49	o-8 a	(S)-2	(S,S)-5	40·10 ⁴ (4)	28	5	>99	94 R
50	p-8 a	(R)-1	(R)-9	" (4)	28	3	>99	91 S
51	o-8 b	(S)-2	(S,S)-5	50·10 ⁵ (50)	28	3	>99	94 R
52	m-8 b	(S)-2	(S)-9	80·10 ⁴ (8)	28	1	96	90 R
53	p-8 b	(S)-2	(S)-9	" (8)	28	16	>99	94 R
54	m-8 c	(R)-1	(R)-9	" (8)	30	3	99	88 S
55	p-8 c	(R)-1	(R)-9	40·10 ⁴ (4)	28	3	>99	92 S
56	p-8 d	(S)-2	(S,S)-5	" (4)	24	1.5	>99	96 R
57	9	(S)-2	(S)-9	10·10 ⁴ (1)	26	18	99	95 R
58	9	(S)-2	(S)-9	50·10 ⁵ (50)	-22	3	98	97 R
61	11	(S)-1	(S)-9	80·10 ⁴ (8)	28	3	97	90 R
62	12	(S)-1	(S)-9	" (8)	28	5	91	98 R
63	13	(R)-1	(R,R)-6	" (8)	-20	20	95	92 S
64	13	(2R,3R)-4	(S,S)-5	40·10 ⁴ (4)	28	19	>99	53 S
65	14	(R)-3	(S)-7	" (4)	28	1	>99	69 S
66	15	(R)-1	(R)-9	80·10 ⁴ (8)	28	1.5	100	94 S
67	16	(S)-1	(R)-5	" (8)	28	2	100	93 R
68	17	(S)-1	(R)-6	" (8)	28	2.5	100	80(cis)
69	18	(S)-1	(S)-9	" (8)	28	20	96	91 (1R,2R)

Example 59

[0066] In the same manner as in Example 1, p-diacylbenzene was used as the reaction substrate, and (S)-isopropyl-2,2-di(p-methoxyphenyl)ethylenediamine was used as the optically active diamine. Reaction was caused under a hydrogen pressure of 40·10⁴ Pa (4 atm) at 28°C for 1.5 hours. The resultant diol had a ratio of optically active compound

to meso compound of 85:15 and the optical active material had an optical purity of over 99%.

Example 60

5 [0067] Reaction was caused in a scale increased to 35 times as large as that of Example 1. From 30 g 1'-acetonaphthone (Compound 10 in Table 1), (R)-1-(1-naphthyl)ethanol was obtained in an amount of 27.90 g. The reaction product was separated by vacuum distillation (98-101°C/67 Pa (0.5 mmHg)), and a pure product of an optical purity of 95% was obtained.

10 Comparative Example 5

[0068] Reaction was carried out under the same conditions as in Example 1, using ethylene diamine in place of (S,S)-diamine. Corresponding optically active alcohol was obtained with an optical purity of 57%.

15 Example 61 - 66

[0069] Under same conditions shown in Example 45, hydrogenation reactions were carried out using unsaturated carbonyl compounds having the carbon-carbon double bonds in each molecular structure as raw materials. Corresponding optically active alcohols were obtained at high yield.

20 [0070] Carbon-carbon multiple bonds were not hydrogenated and carbonyl groups only were hydrogenated. The results are shown in above Table 8.

Example 67

25 [0071] Under the same condition as Example 45, hydrogenation was conducted by using an unsaturated cycloketone (Compound No. 16 shown in Table 6)(0.35g, 2.5mmol), and corresponding optically active unsaturated alcohol was quantitatively obtained. As shown in Table 8, optical purity was 93%ee.

Example 68

30 [0072] Under the same conditions except the addition of KOH of 0.2mmol (0.4M, 2-propamol solution 444μl), racemic 2-methyl cyclohexanone (compound No. 17, shown in Table 6, (0.57g, 5.0mmol) was hydrogenated. The reaction provides optical active alcohol having cis/trans ratio of 97.7:2.3 by procedure of dynamic kinetic resolution at site of 2-asymmetric carbon.

35 [0073] As shown in Table 8, optical purity of cis form was 80%ee.

Example 69

40 [0074] Under the same conditions as Example 68, racemic compound (No. 18, shown in Table 6) (1.05g, 5 mmol) was hydrogenated.

[0075] The reaction was carried out though dynamic kinetic resolution, and provides optically active alcohol having anti/sym ratio of 97.0:3.0.

[0076] As shown in Table 8, optical purity of anti-form was 91%ee.

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Claims

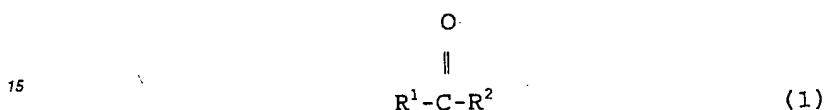
1. A method for producing an alcohol, which comprises the step of causing a carbonyl compound to react with hydrogen in the presence of a homogeneous hydrogenation catalyst which is a transition metal complex catalyst of a group VIII metal, a base and a nitrogen-containing organic compound, wherein said nitrogen-containing organic compound is:

50 a) a mono-amine selected from primary amine, secondary amine or tertiary amine represented by the formula $NR^8R^9R^{10}$; or

55 b) a diamine represented by the formula $R^{11}R^{12}N-Z-NR^{13}R^{14}$ (wherein $R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}$ and R^{14} are each hydrogen, or are the same or different moieties selected from alkyl, cycloalkyl, aryl having 1 to 10 carbon atoms, and cyclic diamine; and Z is a group selected from alkylene, cycloalkylene and arylene having 1 to 6

carbon atoms).

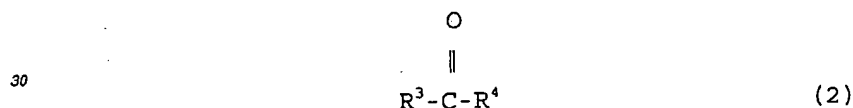
2. A method as claimed in claim 1, wherein said transition metal is a metal selected from the group consisting of rhodium, ruthenium, iridium, palladium and platinum.
3. A method as claimed in claim 1 or claim 2, wherein said base is a hydroxide of an alkali metal or an alkali earth metal or a salt thereof, or a quarternary ammonium salt.
4. A method as claimed in any one of the preceding claims, wherein said carbonyl compound is expressed by the following general formula (1):



(where, R¹ and R² are hydrogen, aromatic monocyclic or polycyclic hydrocarbon groups or hetero-monocyclic or polycyclic groups containing heteroatoms, which may have the same or different substitution groups or a saturated or unsaturated chain or cyclic hydrocarbon group;

R¹ and R² together with the C-atom to which they are attached may also form a cyclic group.

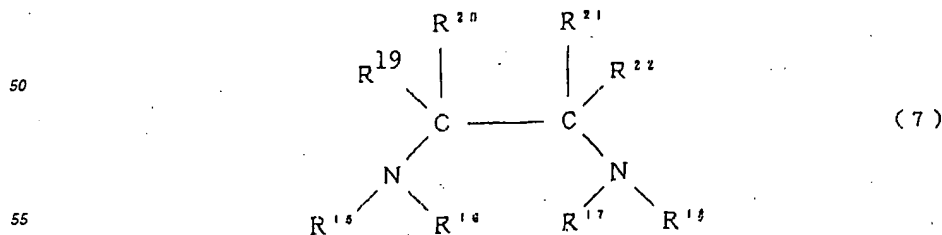
5. A method for producing an optically active alcohol, which comprises the step of subjecting a carbonyl compound expressed by the following general formula (2):



(where, R³ is an aromatic monocyclic or polycyclic hydrocarbon group, a saturated or unsaturated aliphatic or cyclic-hydrocarbon group, or a hetero-monocyclic or polycyclic group containing heteroatoms, which may have a substitution group; and R⁴ is a saturated or unsaturated chain, cyclic or aromatic cyclic hydrocarbon or heterocyclic group, which may have hydrogen or a substitution group; R³ and R⁴ together with the C-atom to which they are attached may also form a cyclic group) to a hydrogenation reaction in the presence of an asymmetric hydrogenation catalyst which is a transition metal complex catalyst of a group VIII metal, and an optically active nitrogen-containing compound, wherein said nitrogen-containing compound is

a) an optically active monoamine in which at least one of the substitution groups is an optically active group and those remaining include hydrogen, or saturated or unsaturated hydrocarbon group or aryl group, or

b) an optically active diamine compound represented by the following general formula (7):



(wherein, R¹⁵, R¹⁶, R¹⁷ and R¹⁸ are hydrogen or saturated or unsaturated hydrocarbon group, aryl group,

urethane group or sulfonyl group, and R¹⁹, R²⁰, R²¹ and R²² are the same or different groups such that carbon atoms bonded with these substitution groups form centers of asymmetry, and represent hydrogen or alkyl group, aromatic monocyclic or polycyclic, saturated or unsaturated hydrocarbon group, and cyclic hydrocarbon group), and a base, thereby producing an optically active alcohol expressed by the following general formula (3):



(where, R³ and R⁴ are the same organic groups as above).

6. A method as claimed in claim 5, wherein said asymmetric hydrogenation catalyst has an optically active ligand.
7. A method as claimed in claim 6, wherein said optically active ligand is a phosphine ligand.
8. A method as claimed in any one of claims 5 to 7, wherein said base is a hydroxide or a salt of an alkali metal or an alkali earth metal, or a quaternary ammonium salt.

Patentansprüche

1. Verfahren zur Herstellung eines Alkohols, das den Schritt aufweist, eine Carbonylverbindung mit Wasserstoff in der Gegenwart eines homogenen Hydrierungskatalysators, der ein Übergangsmetallkomplexbkatalysator eines Metalls aus der Gruppe VIII ist, einer Base und einer stickstoffhaltigen organischen Verbindung zur Reaktion zu bringen, wobei die stickstoffhaltige organische Verbindung:
 - a) ein Monoamin ist, das aus primären Aminen, sekundären Aminen oder tertiären Aminen ausgewählt ist, die durch die Formel NR⁸R⁹R¹⁰ dargestellt sind, oder
 - b) ein Diamin ist, das durch die Formel R¹¹R¹²N-Z-NR¹³R¹⁴ dargestellt ist (wobei R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³ und R¹⁴ jeweils Wasserstoff sind oder gleiche oder verschiedene Gruppen sind, ausgewählt aus Alkyl, Cycloalkyl, Aryl mit 1 bis 10 Kohlenstoffatomen und zyklischen Diaminen, und Z eine Gruppe ausgewählt aus Alkylen, Cycloalkylen und Arylen mit 1 bis 6 Kohlenstoffatomen ist).
2. Verfahren nach Anspruch 1, wobei das Übergangsmetall ein Metall ist, das aus der aus Rhodium, Ruthenium, Iridium, Palladium und Platin bestehenden Gruppe ausgewählt ist.
3. Verfahren nach Anspruch 1 oder 2, wobei die Base ein Hydroxid eines Alkalimetalls oder eines Erdalkalimetalls oder eines Salzes davon oder ein quartäres Ammoniumsalz ist.
4. Verfahren nach einem der vorhergehenden Ansprüche, wobei die Carbonylverbindung durch die folgende allgemeine Formel (1) ausgedrückt ist:



- (dabei sind R¹ und R² Wasserstoff, aromatische monozyklische oder polyzyklische Kohlenwasserstoffgruppen oder heteromonozyklische oder -polyzyklische Gruppen, die Heteroatome aufweisen, die die gleichen oder verschiedene Substituenten oder eine gesättigte oder ungesättigte Kette oder zyklische Kohlenwasserstoffgruppen aufweisen können,

6 R¹ und R² können auch zusammen mit dem C-Atom, an das sie gebunden sind, eine zyklische Gruppe bilden.

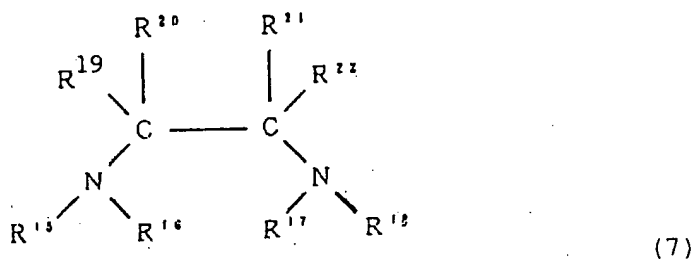
5. Verfahren zur Herstellung eines optisch aktiven Alkohols, das den Schritt aufweist, eine Carbonylverbindung, die durch die folgende allgemeine Formel (2) ausgedrückt ist:



(dabei ist R³ eine aromatische, monozyklische oder polyzyklische Kohlenwasserstoffgruppe, eine gesättigte oder ungesättigte aliphatische oder zyklische Kohlenwasserstoffgruppe oder eine hetero-monozyklische oder -polyzyklische Gruppe mit Heteroatomen, die einen Substituenten aufweisen können, und R⁴ ist eine gesättigte oder ungesättigte Kette, zyklische oder aromatische zyklische Kohlenwasserstoff- oder heterozyklische Gruppe, die Wasserstoff oder einen Substituenten aufweisen kann, R³ und R⁴ können auch zusammen mit dem C-Atom, an das sie gebunden sind, eine zyklische Gruppe bilden) einer Hydrierungsreaktion in Gegenwart eines asymmetrischen Hydrierungskatalysators zu unterwerfen, der ein Übergangskomplekxkatalysator eines Metalls der Gruppe VIII ist, und einer optisch aktiven stickstoffhaltigen Verbindung, wobei die stickstoffhaltige Verbindung:

a) ein optisch aktives Monoamin ist, bei dem mindestens einer der Substituenten eine optisch aktive Gruppe ist und die übrigen Wasserstoff oder gesättigte oder ungesättigte Kohlenwasserstoffgruppen oder Arylgruppen aufweisen, oder

b) eine optisch aktive Diaminverbindung ist, die durch die folgende allgemeine Formel (7) dargestellt ist:



(dabei sind R¹⁵, R¹⁶, R¹⁷ und R¹⁸ Wasserstoff oder eine gesättigte oder ungesättigte Kohlenwasserstoffgruppe, Arylgruppe, Urethangruppe oder Sulfonylgruppe und R¹⁹, R²⁰, R²¹ und R²² sind die gleichen oder verschiedene Gruppen, so daß Kohlenstoffatome, die an diesen Substituenten gebunden sind, asymmetrische Zentren ausbilden und stellen eine Wasserstoff oder Alkylgruppe, aromatische monozyklische oder polyzyklische, gesättigte oder ungesättigte Kohlenwasserstoffgruppe und zyklische Kohlenwasserstoffgruppe dar) und einer Base, zur Herstellung eines optisch aktiven Alkohols, der durch die folgende allgemeine Formel (3) ausgedrückt ist:



(dabei sind R³ und R⁴ die gleichen organischen Gruppen wie oben)

6. Verfahren nach Anspruch 5, wobei der asymmetrische Hydrierungskatalysator einen optisch aktiven Liganden aufweist.

7. Verfahren nach Anspruch 6, wobei der optisch aktive Ligand ein Phosphinligand ist.

8. Verfahren nach einem der Ansprüche 5 bis 7, wobei die Base ein Hydroxid oder ein Salz eines Alkalimetalls oder eines Erdalkalimetalls oder ein quartäres Ammoniumsalz ist.

Revendications

1. Procédé de préparation d'un alcool, comprenant l'étape consistant à faire réagir un composé carbonylé avec de l'hydrogène en présence d'un catalyseur d'hydrogénation homogène consistant en un catalyseur de type complexe de métal de transition dérivé d'un métal du groupe VIII, d'une base et d'un composé organique azoté, ledit composé organique azoté, étant :

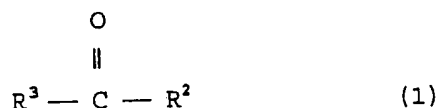
a) une monoamine choisie parmi une amine primaire, une amine secondaire ou une amine tertiaire représentée par la formule $\text{NR}^8\text{R}^9\text{R}^{10}$; ou

b) une diamine représentée par la formule $\text{R}^{11}\text{R}^{12}\text{N}-\text{Z}-\text{NR}^{13}\text{R}^{14}$ (dans laquelle R^8 , R^9 , R^{10} , R^{11} , R^{12} , R^{13} et R^{14} représentent chacun un atome d'hydrogène, ou il s'agit de groupes identiques ou différents choisis parmi les groupes alkyle, cycloalkyle, aryle comportant de 1 à 10 atomes de carbone et diamine cyclique ; et Z représente un groupe choisi parmi les groupes alkylène, cycloalkylène et arylène comportant de 1 à 6 atomes de carbone).

2. Procédé selon la revendication 1, dans lequel ledit métal de transition est un métal choisi parmi le rhodium, le ruthénium, l'iridium, le palladium et le platine.

3. Procédé selon la revendication 1 ou 2, dans lequel ladite base est un hydroxyde de métal alcalin ou de métal alcalino-terreux ou un sel de celui-ci, ou un sel d'ammonium quaternaire.

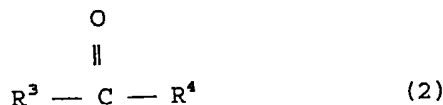
4. Procédé selon l'une quelconque des revendications précédentes, dans lequel ledit composé carbonylé est représenté par la formule générale (1) suivante :



(dans laquelle R^1 et R^2 représentent un atome d'hydrogène, des groupes hydrocarbonés aromatiques mono ou polycycliques ou des groupes mono ou polyhétérocycliques contenant des hétéroatomes, qui peuvent comporter des groupes de substitution identiques ou différents, ou une chaîne saturée ou insaturée, ou un groupe hydrocarboné cyclique ;

R^1 et R^2 peuvent également former ensemble un groupe cyclique avec l'atome de carbone auquel ils sont liés.

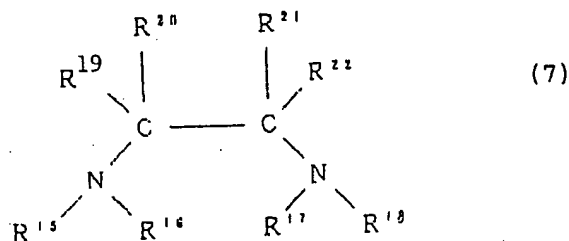
5. Procédé de préparation d'un alcool optiquement actif, comprenant l'étape consistant à soumettre un composé carbonylé représenté par la formule générale (2) suivante :



(dans laquelle R^3 représente un groupe hydrocarboné mono ou polycyclique aromatique, un groupe hydrocarboné

aliphatique ou cyclique saturé ou insaturé, ou un groupe mono ou polyhétérocyclique contenant des hétéroatomes, qui peut comporter un groupe de substitution ; et R⁴ représente une chaîne saturée ou insaturée, un groupe cyclique, ou cyclique aromatique, hydrocarboné ou hétérocyclique, qui peut comporter un atome d'hydrogène ou un groupe de substitution ; R³ et R⁴ peuvent également former ensemble un groupe cyclique avec l'atome de carbone auquel ils sont liés) à une réaction d'hydrogénation en présence d'un catalyseur d'hydrogénation asymétrique consistant en un catalyseur de type complexe de métal de transition dérivé d'un métal du groupe VIII, et un composé azoté optiquement actif, ledit composé azoté étant :

- a) une monoamine optiquement active dans laquelle au moins l'un des groupes de substitution est un groupe optiquement actif, et ceux restants comprennent un atome d'hydrogène, ou un groupe hydrocarboné saturé ou insaturé, ou un groupe aryle, ou
b) un composé diaminé optiquement actif représenté par la formule générale (7) suivante :



(dans laquelle R¹⁵, R¹⁶, R¹⁷ et R¹⁸ représentent un atome d'hydrogène ou un groupe hydrocarboné saturé ou insaturé, un groupe aryle, un groupe uréthane ou un groupe sulfonyle, et R¹⁹, R²⁰, R²¹ et R²² sont des groupes identiques ou différents tels que les atomes de carbone liés à ces groupes de substitution forment des centres d'asymétrie, et ils représentent un atome d'hydrogène ou un groupe alkyle, un groupe hydrocarboné mono ou polycyclique aromatique, saturé ou insaturé, et un groupe hydrocarboné cyclique), et une base, de façon à produire un alcool optiquement actif représenté par la formule générale (3) suivante :



(dans laquelle R³ et R⁴ sont les mêmes groupes organiques que ci-dessus).

6. Procédé selon la revendication 5, dans lequel ledit catalyseur d'hydrogénation asymétrique comporte un ligand optiquement actif.
7. Procédé selon la revendication 6, dans lequel ledit ligand optiquement actif est un ligand phosphine.
8. Procédé selon l'une quelconque des revendications 5 à 7, dans lequel ladite base est un hydroxyde ou un sel de métal alcalin ou d'un métal alcalino-terreux, ou un sel d'ammonium quaternaire.

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